

REMARKS

Claims 1-8, 10, 11, 13, and 16-28 are pending in the present application. By virtue of this response, claims 7 and 18 have been cancelled, and claims 1, 2, 3, and 11 have been amended. Accordingly, claims 1-6, 8, 10, 11, 13, 16, 17, and 19-28 are currently under consideration. Support for amended claims 1, 3, and 11 is provided throughout the specification, such as at page 34, lines 14-31. Support for amended claim 2 is provided throughout the specification, such as at page 10, lines 1-4, and page 14, lines 7 and 8. No new matter has been added.

With respect to all claim amendments, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in a future continuation and/or divisional application.

Information Disclosure Statement

Applicants thank the Examiner for having considered the references previously submitted in the Information Disclosure Statement.

Request for Reconsideration of the Finality of the Office Action

Applicants respectfully request the removal of the finality of the Office Action mailed January 23, 2008. MPEP § 706.07(a) states:

Under present practice, second or any subsequent actions on the merits shall be final, except where the examiner introduces a new ground of rejection that is neither necessitated by applicant's amendment of the claims, nor based on information submitted in an information disclosure statement filed during the period set forth in 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p).

The new rejection under 35 U.S.C. § 103(a) in this Office Action is based on the newly cited references Wadsworth *et al.* (U.S. Pat. No. 5,720,936), Countouriotis *et al.* (Stem Cells 20:215-229, 2002), and Capecchi *et al.* (U.S. Pat. No. 5,627,059). This rejection was neither necessitated by

Applicants' amendment of the claims nor based on information submitted in an Information Disclosure Statement. In particular, claim 15 as filed specified that the transgenic animal of claim 1 is a mouse. In the interest of expediting prosecution, Applicants amended claim 1 (from which all the other claims depend from or refer to) to specify that the transgenic animal is a mouse in the Amendment filed November 6, 2007. The Amendment filed November 6, 2007 did not necessitate the new rejection under 35 U.S.C. § 103(a) in this Office Action since claims to a transgenic mouse were already pending. Thus, this rejection could have been made in the previous Office Action mailed June 6, 2007. Accordingly, the finality of the Office Action mailed January 23, 2008 is improper.

In the event this request is denied, Applicants request the Examiner to notify Applicants' attorneys as soon as possible, so that Applicants can act to preserve the pendency of the present application.

Claim Objections

Claim 7

Claim 7 stands objected to under 37 CFR § 1.75(c), as allegedly being of improper dependent form for failing to further limit the subject matter of a previous claim.

In the interest of expediting prosecution, claim 7 has been canceled. Accordingly, this rejection is now moot. Applicants respectfully request that this rejection be withdrawn.

Claim 11

Claim 11 stands objected to. The Examiner states that the phrase "B lymphocytes and/or pre-B" should be inserted after "said."

In response, Applicants have amended claim 11 to refer to "B lymphocytes and/or pre-B cells." Accordingly, this rejection should be withdrawn.

Claim 18

Claim 18 stands objected to under 37 CFR § 1.75(c), as allegedly being in improper dependent form for failing to further limit the subject matter of a previous claim.

In the interest of expediting prosecution, claim 18 has been canceled. Accordingly, this rejection is now moot. Applicants respectfully request that this rejection be withdrawn.

Claims 24-28

Claims 24-28 stand objected to under 37 CFR § 1.75, as allegedly being a substantial duplicate of claims 8, 10, 11, 20, and 21, respectively.

MPEP § 706.03(k) states that “court decisions have confirmed applicant's right to restate (i.e., by plural claiming) the invention in a reasonable number of ways. Indeed, a mere difference in scope between claims has been held to be enough.”

Claims 24 and 25 are broader in scope than claim 8 and 20 because they require fewer steps. Similarly Claims 26-28 are broader in scope than claims 10, 11, and 21 because they require fewer steps. Due to the difference in scope between these claims, claims 24-26 are no substantial duplicates of claims 8, 10, 11, 20, and 21. In light of these clarifying remarks, this rejection should be withdrawn.

Claim Rejection Under 35 U.S.C. § 103(a)

Claims 1-8, 10, 11, 13, and 16-28

Claims 1-8, 10, 11, 13, and 16-28 stand rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Wadsworth *et al.* (U.S. Pat. No. 5,720,936), in view of Countouriotis *et al.* (Stem Cells 20:215-229, 2002) and Capecchi *et al.* (U.S. Pat. No. 5,627,059).

Applicants respectfully traverse this rejection.

As amended, claim 1 (from which all the other claims depend from or refer to) is directed to a transgenic mouse whose genome comprises a nucleotide sequence encoding human CD20 such that human CD20 is expressed on the surface of a B lymphocyte and/or pre-B cell of the mouse.

None of the cited references, alone or together, teach or suggest the generation of a transgenic mouse that expresses CD20 on the surface of a B lymphocyte and/or pre-B cell. As stated by the Examiner, Wadsworth teaches “a different mouse model expressing different disease genes,” such as APP. Capecchi discusses transgenic mice, but also does not teach or suggest the production of a transgenic mouse expressing human CD20. Countouriotis discloses an anti-CD20 antibody for the treatment of lymphoma. Countouriotis does not teach or suggest the generation or use of a transgenic mouse expressing human CD20. The Examiner has not provided any evidence that one skilled in the art would have been motivated to modify the transgenic mice of Wadsworth and Capecchi based on the teachings of Countouriotis to produce a transgenic mouse that expresses CD20 on the surface of a B lymphocyte and/or pre-B cell.

A skilled artisan would not have had a reasonable expectation of success for the generation of a transgenic mouse that expresses CD20 on the surface of a B lymphocyte and/or pre-B cell. To be useful as a model for identifying agents capable of killing B lymphocytes and/or pre-B cells that express human CD20, a transgenic mouse must express human CD20 on a sufficient number of B lymphocytes and/or pre-B cells for the decrease in the number of B lymphocytes and/or pre-B cells due to the agent to be detected. Because of the unpredictability in the field of transgenic mice, there was no reasonable expectation of success for the expression of the human CD20 transgene in the desired cell types (such as B lymphocytes and/or pre-B cells) in an amount sufficient for identifying agents that kill human CD20-expressing B lymphocytes and/or pre-B cells.

Applicants generated human CD20 transgenic mice and found that human CD20 is expressed on mature, pre-B, and immature B-cells in the blood, bone marrow, spleen, lymph nodes, and Peyer's patches of human CD20 transgenic mice (see, *e.g.*, Example 1, pages 31-34). The

expression level of human CD20 on the transgenic cells was about 40% of that of CD20 on human cells (see, for example, page 34, lines 16 and 17). Treatment of the transgenic mice with an anti-human CD20 antibody resulted in depletion of B cells in the peripheral blood, mature peripheral lymph node B cells, and T2 and follicular B cells in the spleen (see, for example, page 33, lines 6-8, and Figures 8-11).

Accordingly, the presently claimed invention is nonobvious over Wadsworth in view of Countouriotis and Capecchi.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 146392000401. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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